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Mlostoń, Grzegorz ; Grzelak, Paulina ; Heimgartner, Heinz

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# Hetero-Diels-Alder reactions of hetaryl-thiochalcones with acetylenic dienophiles

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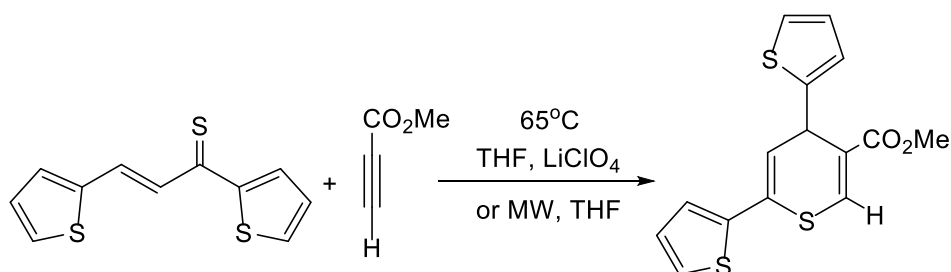
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## Abstract

Hetaryl-substituted thiochalcones react with acetylenic mono- and diesters in THF solution in the presence of LiClO<sub>4</sub> at 65°C to give, after 24 h, 4*H*-thiopyran carboxylates and dicarboxylates, respectively, in moderate to good yields. The same reactions were performed also in THF solution without catalyst under microwave irradiation. In that case, the reaction time was reduced to three minutes and, in most cases, an improvement of the yield of the [4+2]-cycloadduct was observed. The reactions with methyl propiolate occurred regioselectively and the 3-carboxylates were formed exclusively.

## Graphical Abstract



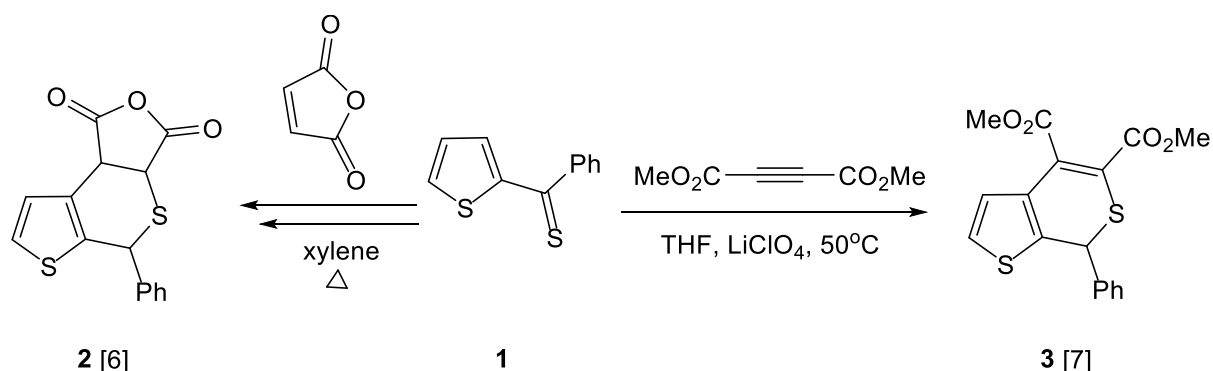
**Keywords:** chalcones, thiochalcones, acetylenic dienophiles, hetero-Diels-Alder reactions, 4*H*-thiopyrans, microwave irradiation

## 1. Introduction

Hetero-Diels-Alder reactions of heterodienes are widely applied for the synthesis of six-membered heterocycles including important intermediates in natural product synthesis [1,2]. In that case, the asymmetric version is of special importance [3]. The most frequently reported hetero-Diels-Alder reactions belong to the so-called aza- or oxa-types with the C=N or C=O units in the diene or dienophile. In contrast, examples for thia-type hetero-Diels-Alder reactions are less well-known. Whereas reactions of dienes with diaryl thioketones leading to dihydrothiopyrans were studied to some extent [4], the [4+2]-cycloadditions with thiochalcones are rarely described [5]. In most cases the studied thia-hetero-Diels-Alder reactions comprised reactions of other types of thia-heterodienes, such as enaminothiones [5] or  $\alpha,\beta$ -unsaturated thioamides [5,6]. In a series of recent publications, 5-arylidene-4-thioxo-2-thiazolidinones were used as more complex 1-thia-1,3-dienes in reactions with diverse ethylenic dipolarophiles [7-10]. Furthermore, a few thia-hetero-Diels-Alder reactions of diverse 1-thia-1,3-dienes (but not thiochalcones !) with propiolates [6,7], benzyne [11], and an intramolecular reaction with a propargyl ether [12] are known.

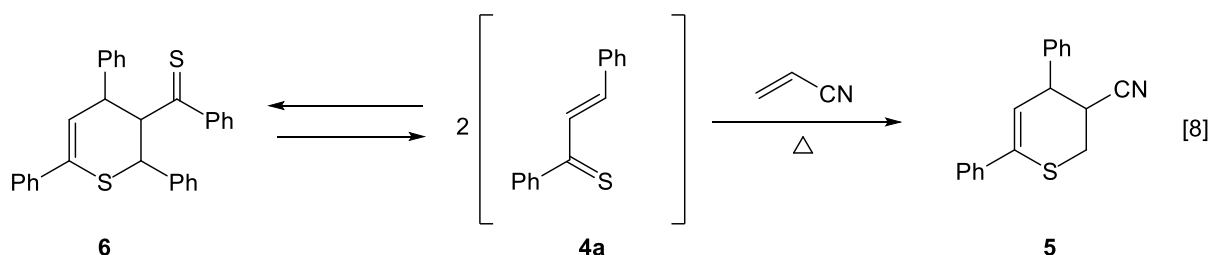
Kinetic studies of the [4+2]-cycloadditions of cyclic and acyclic dienes with diaryl thioketones led to the introduction of the name “superdienophiles” for the latter [4].

An interesting class of S-heterodienes are hetaryl thioketones of type **1**, which react with activated ethylene and acetylene derivatives yielding fused thiopyran derivatives of type **2** and **3**, respectively [13,14] (Scheme 1).



**Scheme 1.** Hetero-Diels-Alder reactions with hetaryl thioketone **1**.

Thiochalcones **4**, which are  $\alpha,\beta$ -unsaturated thioketones, form a class of attractive thiadienes. They have rarely been explored in hetero-Diels-Alder reactions [5], mainly with ethylenic dienophiles. For example, the reaction of 2,4-diphenyl-1-thiabuta-1,3-diene (**4a**) with acrylonitrile led to the dihydrothiopyran **5** in a regioselective manner [15] (Scheme 2). The reactive thiochalcone **4a** was generated in-situ by thermolysis of its dimer **6**.



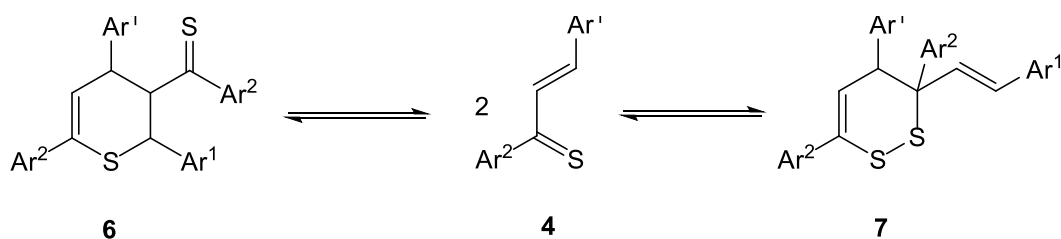
**Scheme 2.** [4+2]-Cycloaddition of diphenylchalcone with acrylonitrile.

Remarkably, thiochalcone **4a** reacted also with the electron-rich *n*-butyl vinyl ether to give the [4+2]-cycloadduct in a Diels-Alder reaction with inverse electron demand [16]. Furthermore, the reaction of dimethyl acetylene dicarboxylate (DMAD, **8a**) with in-situ-generated thiochalcones yielded 4*H*-thiopyrans [17]. In the case of enaminothiones, the reactions with methyl propiolate (MP, **8b**) occurred regioselectively leading to 4-amino-4*H*-thiopyran-3-carboxylates as primary products, which upon heating isomerized to 2-amino-2*H*-thiopyran-3-carboxylates [18,19].

Due to our continuing interest in the chemistry of hetaryl thioketones, a series of new thiochalcones with hetaryl groups was prepared and subsequently applied in hetero-Diels-Alder reactions with DMAD and MP.

## 2. Results and discussion

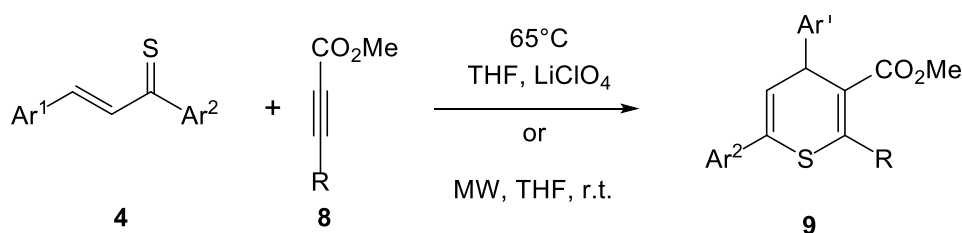
Hetaryl thiochalcones **4b–g** (Table 1) were prepared from the corresponding chalcones by treatment with Lawesson's reagent in refluxing THF solution and isolated after chromatographic workup. The  $^1\text{H}$  NMR spectra of analytically pure samples showed that they exist in  $\text{CDCl}_3$  solution in equilibrium with dimeric forms similar to the observations with diarylchalcones [20] (Scheme 3).



**Scheme 3.** Equilibrium of thiochalcones with dimers.

Nevertheless, the cycloaddition reactions performed with acetylenic dienophiles **8** occur smoothly in THF solution in the presence of catalytic amounts of  $\text{LiClO}_4$ . After 24 h of heating at  $65^\circ\text{C}$  in a glass tube with a screw cap, the reactions were complete and the  $^1\text{H}$  NMR analysis evidenced the presence of a single product in all cases. The spectroscopic data confirmed the structure of 4*H*-thiopyrane derivatives **9** (Scheme 4, Table 1). Thus, in the case of the products formed from DMAD (**8a**) and **4b** and **4d**, respectively, two isomeric compounds were identified. In the first one, **9b**, the  $^1\text{H}$  NMR spectrum showed two characteristic doublets at 6.24 and 5.27 ppm with  $J = 6.6$  Hz attributed to HC(5) and HC(4) of the thiopyran ring. The analogous set of signals in the spectrum of **9d** appeared at 6.22 and 4.85 ppm ( $J = 6.6$  Hz). In the  $^{13}\text{C}$  NMR spectra, a significant difference in the chemical shift of HC(4) was observed. Whereas in **9d** the signal appeared at 44.5 ppm, it was shifted upfield to 38.6 ppm in **9b**.

The structure of the products obtained regioselectively in the experiments with methyl propiolate (**8b**) were unambiguously established on the basis of the  $^1\text{H}$  NMR spectra. In all compounds **9h–n**, the signals of HC(4) appeared as a doublet in the range of 4.81–5.26 ppm. In addition, the singlet for HC(2) was located in a narrow range at 7.67–7.90 ppm. The same regioselectivity was observed in the reaction of the parent thiochalcone **4a** with **8b**, and the structure **9h** was elucidated spectroscopically. The comparison of the chemical shifts observed in the  $^{13}\text{C}$  NMR spectra of **9h** and **9i** evidences that the shielding effect of the thiophen-2-yl substituent is stronger than in the case of the phenyl ring.



**Scheme 4.** Hetero-Diels-Alder reactions of thiochalcones **4** with acetylene carboxylates.

**Table 1.** Synthesis of 4*H*-thiopyrans **9** via hetero-Diels-Alder reaction

Acetylene <b>8</b> R	Thiochalcone <sup>a)</sup> <b>4</b> Ar <sup>1</sup> Ar <sup>2</sup>		Thiopyran <b>9</b>	Yield [%] <sup>b)</sup>	
				Method A	Method B
<b>a</b> CO <sub>2</sub> Me	<b>a</b> Ph	Ph	<b>a</b> [10]	80	93
<b>a</b> CO <sub>2</sub> Me	<b>b</b> Thi	Ph	<b>b</b>	85	86
<b>a</b> CO <sub>2</sub> Me	<b>c</b> Fur	Ph	<b>c</b>	77	95
<b>a</b> CO <sub>2</sub> Me	<b>d</b> Ph	Thi	<b>d</b>	36	48
<b>a</b> CO <sub>2</sub> Me	<b>e</b> Ph	Fur	<b>e</b>	6	<sup>c)</sup>
<b>a</b> CO <sub>2</sub> Me	<b>f</b> Ph	Sel	<b>f</b>	16	56
<b>a</b> CO <sub>2</sub> Me	<b>g</b> Thi	Thi	<b>g</b>	67	<sup>d)</sup>
<b>b</b> H	<b>a</b> Ph	Ph	<b>h</b> [10]	85	93
<b>b</b> H	<b>b</b> Thi	Ph	<b>i</b>	92	92
<b>b</b> H	<b>c</b> Fur	Ph	<b>j</b>	94	98
<b>b</b> H	<b>d</b> Ph	Thi	<b>k</b>	48	71
<b>b</b> H	<b>e</b> Ph	Fur	<b>l</b>	6	<sup>c)</sup>
<b>b</b> H	<b>f</b> Ph	Sel	<b>m</b>	15	60
<b>b</b> H	<b>g</b> Thi	Thi	<b>n</b>	97	<sup>d)</sup>

<sup>a)</sup> Ph = Phenyl; Thi = Thiophen-2-yl; Fur = Furan-2-yl; Sel = Selenophen-2-yl

<sup>b)</sup> Yield of isolated product. Method A: THF, LiClO<sub>4</sub>, 65°C; Method B: THF, MW, r.t.

<sup>c)</sup> Only decomposition products were obtained

<sup>d)</sup> Experiment has not been performed

The microwave technique has been widely applied to accelerate organic reactions. In the present study, the reactions of DMAD (**8a**) and MP (**8b**) with hetaryl thiochalcones **4** were carried out in THF solutions under microwave irradiations (Method B). As a matter of fact, the reaction times were drastically reduced (ca. 3 min) and the yields of the products were higher (Table 1). Only in the case of thiochalcone **4e** with the furan-2-yl group at C(1), decomposition was observed, similarly to the reaction performed under standard conditions.

### 3. Conclusions

Hetaryl thiochalcones bearing the hetaryl group either at C(2) or C(4) of the 1-thiabuta-1,3-diene structure react smoothly with acetylene carboxylates yielding the expected 4*H*-thiopyran derivatives. In the case of methyl propiolate (MP), the [4+2]-cycloaddition occurs regioselectively yielding thiopyran-3-carboxylates. Whereas thermal reactions performed at 65°C in the presence of LiClO<sub>4</sub> as a catalyst required ca. 24 h for completion, the non-catalyzed microwave-supported reactions were finished after ca. 3 min.

### 4. Experimental Design

#### 4.1. General

Melting points were determined in a capillary using a MEL-TEMP II apparatus (*Aldrich*) and are uncorrected. IR spectra were recorded with a FT-IR NEXUS spectrophotometer as KBr pellets; absorptions ( $\nu$ ) in cm<sup>-1</sup>. <sup>1</sup>H and <sup>13</sup>C NMR spectra were measured on a Bruker Avance III (<sup>1</sup>H at 600 and <sup>13</sup>C at 150 MHz) instrument in CDCl<sub>3</sub>; chemical shifts ( $\delta$ ) are given in ppm, coupling constants (*J*) in Hz. The multiplicity of the <sup>13</sup>C signals was deduced from DEPT, supported by <sup>1</sup>H-<sup>13</sup>C HMQC spectra. <sup>1</sup>H NMR data are presented as follows: chemical shift, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant, integration. The mass spectra were recorded on a Finnigan MAT-95(ESI), Bruker maxis (HR-ESI), or SYNAPT G2-S HMDS (HR MALDI-TOF) instrument. Elemental analyses were performed in the Microanalytical Laboratory of the Chemistry Faculty in Łódź. Microwave experiments were carried out with CEM Focused Microwave type Discover SPD. Applied reagents such as dimethyl acetylenedicarboxylate (DMAD, **8a**), methyl propiolate (MP, **8b**), inorganic reagents, and solvents are commercially available (*Aldrich*) and were used as received.

## 4.2. Starting materials

Chalcones were obtained from aryl methyl ketones and aromatic aldehydes in the presence of NaOH according to the known general procedure [21]. *1,3-Diphenylpropen-3-one*: Pale yellow crystals; yield: 91%; m.p. 55.5–56.0°C (C<sub>2</sub>H<sub>5</sub>OH) ([22]: m.p. 56.0°C). *1-Phenyl-3-(thiophen-2-yl)prop-2-en-1-one*: Yellow crystals; yield: 84%; m.p. 58.0–59.0°C (C<sub>2</sub>H<sub>5</sub>OH) ([23]: m.p. 58.0–59.0°C). *3-Phenyl-1-(thiophen-2-yl)prop-2-en-1-one*: Pale yellow crystals; yield: 78%; m.p. 82.5–83.0°C (C<sub>2</sub>H<sub>5</sub>OH) ([24], m.p. 82°C). *3-(Furan-2-yl)-1-phenylprop-2-en-1-one*: Pale yellow crystals; yield: 85%; m.p. 42.0–42.5°C (C<sub>2</sub>H<sub>5</sub>OH) ([25], m.p. 40.0°C). *1-(Furan-2-yl)-3-phenylprop-2-en-1-one*: Pale yellow crystals; yield: 71%; m.p. 86.0–87.0°C (C<sub>2</sub>H<sub>5</sub>OH) ([26]: m.p. 87.0–88.0°C). *3-Phenyl-1-(selenophen-2-yl)prop-2-en-1-one*: Pale yellow crystals; yield: 82%; m.p. 81.5–82.0°C (C<sub>2</sub>H<sub>5</sub>OH) ([27]: m.p. 81.0–82.5°C). *1,3-Di(thiophen-2-yl)prop-2-en-1-one*: Yellow crystals; yield: 70%; m.p. 95.5–96.0°C (C<sub>2</sub>H<sub>5</sub>OH) ([25]: m.p. 94–95°C).

## 4.3. Synthesis of hetaryl thiochalcones (4a–g)

A solution of 5 mmol of the corresponding chalcone and 5.1 mmol of Lawesson's reagent in 10 mL of dry THF were placed in a two-necked flask. The mixture was heated under argon at reflux for 3 h. Then, the solvent was evaporated in vacuo and the residue was purified chromatographically, using as the eluent a mixture of petroleum ether and chloroform (1:1). The <sup>1</sup>H NMR spectra showed the presence of variable mixtures of monomers and dimers of the thiocalcones **4**.

### *1,3-Diphenylpropen-3-thione (4a)*

Purple solid; yield: 672 mg (65%); m.p. 129.0–130.0°C (lit. [15]: m.p. 134.0–135.0°C). Anal. calcd for C<sub>15</sub>H<sub>12</sub>S (224.33): C 80.30, H 5.40, S 14.29; found: C 80.14, H 5.64, S 14.37.

### *1-Phenyl-3-(thiophen-2-yl)prop-2-en-1-thione (4b)*



Purple solid; yield: 862.5 mg (75%); m.p. 60.5–61.0°C. Anal. calcd for  $C_{13}H_{10}S_2$  (230.35): C 67.78, H 4.38, S 27.83; found: C 67.69, H 4.54, S 27.84.

*3-(Furan-2-yl)-1-phenylprop-2-en-1-thione (4c)*

Purple solid; yield: 770.4 mg (72%); m.p. 59.0–59.5°C. Anal. calcd for  $C_{13}H_{10}OS$  (214.29): C 72.86, H 4.71, S 14.96; found: C 72.76, H 4.71, S 14.81.

*3-Phenyl-1-(thiophen-2-yl)prop-2-en-1-thione (4d)*

Green solid; yield: 931.5 mg (81%); m.p. 76.0–76.5°C. Anal. calcd for  $C_{13}H_{10}S_2$  (230.35): C 67.78, H 4.38, S 27.83; found: C 67.59, H 4.56, S 27.73.

*1-(Furan-2-yl)-3-phenylprop-2-en-1-thione (4e)*

Green solid; yield: 802.5 mg (75%); m.p. 110.0–110.5°C. Anal. calcd for  $C_{13}H_{10}OS$  (214.29): C 72.86, H 4.71, S 14.96; found: C 72.86, H 4.97, S 14.70.

*3-Phenyl-1-(selenophen-2-yl)prop-2-en-1-thione (4f)*

Green solid; yield: 844.5 mg (61%); m.p. 115.0–115.5°C. Anal. calcd for  $C_{13}H_{10}SeS$  (277.25): C 56.31, H 3.64, S 11.56; found: C 56.16, H 3.89, S 11.58.

*1,3-Di(thiophen-2-yl)prop-2-en-1-thione (4g)*

Green solid; yield: 840 mg (70%); m.p. 80.0–80.5°C. Anal. calcd for  $C_{11}H_8S_3$  (236.37): C 55.89, H 3.42, S 40.69; found: C 55.73, H 3.67, S 40.53.

#### 4.4. Reaction of thiochalcones **4** with acetylenic dienophiles **8** – General procedures

**Method A:** A solution of 1 mmol of the corresponding thiochalcone **4**, 1.1 mmol of the corresponding acetylenic dienophile **8** and 10 mol% of  $LiClO_4$  in 1 mL of dry THF were placed in a thick-wall glass tube, which then was closed with a screw cap. The mixture was

heated at 65°C for 24 h. The solvent was evaporated in vacuo. The residue was purified chromatographically, using as the eluent a mixture of petroleum ether and ethyl acetate (1:1).

**Method B:** A solution of 1 mmol of the corresponding thiochalcone and 1.1 mmol of the corresponding acetylenic dienophile **8** in 1 mL of dry THF were placed in a reaction tube. The reaction tube was sealed and transferred to the microwave reactor Discover SPD (150 W, 3 min). After cooling the reaction mixture to room temperature, the solvent was evaporated in vacuo. The residue was purified chromatographically, using as the eluent a mixture of petroleum ether and ethyl acetate (1:1).

*Dimethyl 4,6-diphenyl-4H-thiopyran-2,3-dicarboxylate (9a)* [17]

Yellow oil; yield (method B): 340.4 mg (93%). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>): 3.58, 3.77 (2s, 6H, 2OCH<sub>3</sub>), 4.82 (*d*, *J* = 6.6 Hz, 1H), 6.06 (*d*, *J* = 6.6 Hz, 1H), 7.16–7.18 (*m*, 1H), 7.23–7.26 (*m*, 5H), 7.29–7.31 (*m*, 2H), 7.38–7.39 (*m*, 2H).

*Dimethyl 6-phenyl-4-(thiophen-2-yl)-4H-thiopyran-2,3-dicarboxylate (9b)*

Orange oil; yield (method B): 319.9 mg (86%). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>): 3.77, 3.87 (2s, 6H, 2OCH<sub>3</sub>), 5.27 (*d*, *J* = 6.6 Hz, 1H), 6.24 (*d*, *J* = 6.6 Hz, 1H), 6.94–6.95 (*m*, 1H), 7.01 (*d*, *J* = 3.6 Hz, 1H), 7.20 (*d*, *J* = 4.8 Hz, 1H), 7.36–7.38 (*m*, 3H), 7.51–7.52 (*m*, 2H). <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>): 38.6 (C(4)), 52.6, 53.2 (2OCH<sub>3</sub>), 126.1, 132.6, 135.5, 136.5, 144.1 (5C(sp<sup>2</sup>)), 119.9, 125.1, 126.9, 127.0, 128.8, 129.2 (9CH(sp<sup>2</sup>)), 165.2, 165.4 (2C=O). IR (film): 3025w, 2952w, 1736, 1715vs (2ν<sub>C=O</sub>), 1597w, 1492w, 1442w, 1337w, 1261s, 1021w, 761w, 694m. Anal. calcd for C<sub>19</sub>H<sub>16</sub>O<sub>4</sub>S<sub>2</sub> (372.47): C 61.26, H 4.34, S 17.21; found: C 61.12, H 4.5, S 17.14.

*Dimethyl 4-(furan-2-yl)-6-phenyl-4H-thiopyran-2,3-dicarboxylate (9c)*

Orange oil; yield (method B): 338.2 mg (95%). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>): 3.77, 3.88 (2s, 6H, 2OCH<sub>3</sub>), 5.12 (*d*, *J* = 6.6 Hz, 1H), 6.17–6.19 (*m*, 2H), 6.29–6.30 (*m*, 1H), 7.35–7.37 (*m*, 4H), 7.49–7.51 (*m*, 2H). <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>): 37.9 (C(4)), 52.7, 53.3 (2OCH<sub>3</sub>), 124.6, 133.7, 136.4, 136.6, 152.6 (5C(sp<sup>2</sup>)), 106.7, 110.5, 117.5, 126.9, 128.8, 129.2, 142.5 (9CH(sp<sup>2</sup>)), 165.2, 165.6 (2C=O). IR (film): 3056w, 2949w, 1733, 1714vs (2ν<sub>C=O</sub>), 1594w,

1492<sub>w</sub>, 1442<sub>w</sub>, 1255<sub>s</sub>, 1011<sub>m</sub>, 764<sub>m</sub>, 698<sub>w</sub>. Anal. calcd for C<sub>19</sub>H<sub>16</sub>O<sub>5</sub>S (356.41): C 64.02, H 4.53, S 8.99; found: C 63.87, H 4.65, S 8.85.

*Dimethyl 4-phenyl-6-(thiophen-2-yl)-4H-thiopyran-2,3-dicarboxylate (9d)*

Orange oil; yield (method B): 178.6 mg (48%). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>): 3.66, 3.86 (2s, 6H, 2OCH<sub>3</sub>), 4.85 (*d*, *J* = 6.6 Hz, 1H), 6.22 (*d*, *J* = 6 Hz, 1H), 6.99 (*dd*, *J* = 4.8, 3.6 Hz, 1H), 7.18–7.19 (*m*, 1H), 7.23–7.27 (*m*, 2H), 7.30–7.36 (*m*, 4H). <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>): 44.5 (C(4)); 52.6, 55.3 (2OCH<sub>3</sub>), 125.0, 129.1, 133.0, 139.8, 141.3 (5C(sp<sup>2</sup>)), 119.7, 125.2, 125.8, 127.7, 127.8, 128.1, 128.8 (9CH(sp<sup>2</sup>)), 166.2, 164.9 (2C=O). IR (film): 3028<sub>w</sub>, 2952<sub>w</sub>, 1730, 1721<sub>vs</sub> (2ν<sub>C=O</sub>), 1597<sub>w</sub>, 1451<sub>w</sub>, 1429<sub>m</sub>, 1258<sub>s</sub>, 1023<sub>m</sub>, 761<sub>w</sub>, 698<sub>m</sub>. Anal. calcd for C<sub>19</sub>H<sub>16</sub>O<sub>4</sub>S<sub>2</sub> (372.47): C 61.26, H 4.34, S 17.21; found: C 61.43, H 4.58, S 17.19.

*Dimethyl 6-(furan-2-yl)-4-phenyl-4H-thiopyran-2,3-dicarboxylate (9e)*

Yield (method A): 6%. The compound was identified only on the basis of the <sup>1</sup>H NMR spectra and could not be isolated in pure form. The yield was calculated based on the <sup>1</sup>H NMR spectra of the crude mixture using a weighed amount of 1,1,2,2-tetrachloroethane as a standard. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>): 3.86, 3.66 (2s, 6H, 2OCH<sub>3</sub>), 4.85 (*d*, *J* = 6.6 Hz, 1H), 6.40–6.41 (*m*, 2H), 6.46 (*d*, *J* = 3.0 Hz, 1H), 7.28–7.33 (*m*, 3H), 7.35–7.37 (*m*, 3H).

*Dimethyl 4-phenyl-6-(selenophen-2-yl)-4H-thiopyran-2,3-dicarboxylate (9f)*

Orange oil; yield (method B): 234.5 mg (56%). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>): 3.67, 3.86 (2s, 6H, 2OCH<sub>3</sub>), 4.84 (*d*, *J* = 6.6 Hz, 1H), 6.18 (*d*, *J* = 6.6 Hz, 1H), 7.22–7.27 (*m*, 2H), 7.31–7.34 (*m*, 2H), 7.36–7.37 (*m*, 3H), 7.92 (*d*, *J* = 5.4 Hz, 1H). <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>): 44.7 (C(4)), 52.6, 55.3 (2OCH<sub>3</sub>), 127.0, 128.8, 133.2, 141.2, 144.6 (5C(sp<sup>2</sup>)), 120.3, 127.4, 127.8, 128.2, 129.1, 130.2, 131.1 (9CH(sp<sup>2</sup>)), 164.9, 166.2 (2C=O). IR (film): 3025<sub>w</sub>, 2952<sub>w</sub>, 1736, 1726<sub>vs</sub> (2ν<sub>C=O</sub>), 1600<sub>w</sub>, 1454<sub>w</sub>, 1435<sub>m</sub>, 1261<sub>s</sub>, 1021<sub>w</sub>, 786<sub>w</sub>, 697<sub>m</sub>. Anal. calcd for C<sub>19</sub>H<sub>16</sub>SeO<sub>4</sub>S (419.37): C 54.41, H 3.85, S 7.64; found: C 54.67, H 3.86, S 7.43.

*Dimethyl 4,6-bis(thiophen-2-yl)-4H-thiopyran-2,3-dicarboxylate (9g)*

Yield (method A): 253.2 mg (67%). The compound was identified only on the basis of the  $^1\text{H}$  NMR spectra and could not be isolated in pure form. The yield was calculated based on the  $^1\text{H}$  NMR spectra of crude mixture using a weighed amount of 1,1,2,2-tetrachloroethane as a standard.  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ ): 3.77, 3.86 (2s, 6H,  $2\text{OCH}_3$ ), 5.20 (d,  $J = 20.4$  Hz, 1H), 6.30 (d,  $J = 20.4$  Hz, 1H), 6.91–7.04 (m, 3H), 7.17–7.30 (m, 3H).

*Methyl 4,6-diphenyl-4H-thiopyran-3-carboxylate (9h)*

Yellow solid; yield (method B): 286.4 mg (93%); m.p. 76.2–76.7°C (chromatographic purification).  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ ): 3.61 (s, 3H,  $\text{OCH}_3$ ), 4.81 (d,  $J = 6$  Hz, 1H), 6.10 (d,  $J = 6.6$  Hz, 1H), 7.12–7.16 (m, 1H), 7.21–7.27 (m, 5H), 7.33–7.37 (m, 4H), 7.67 (s, 1H).  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ ): 41.5 (C(4)), 52.0 ( $\text{OCH}_3$ ), 123.9, 129.2, 137.7, 144.2 ( $4\text{C}(\text{sp}^2)$ ), 122.3, 126.5, 127.2, 128.1, 128.77, 128.81, 128.84, 132.8 ( $12\text{CH}(\text{sp}^2)$ ), 165.2 (C=O). IR (KBr): 3025w, 2955w, 1708vs ( $\nu_{\text{C=O}}$ ), 1594w, 1429m, 1249s, 1046w, 755m, 694m. Anal. calcd for  $\text{C}_{19}\text{H}_{16}\text{O}_2\text{S}$  (308.41): C 73.99, H 5.24, S 10.39; found: C 74.06, H 5.47, S 10.49.

*Methyl 6-phenyl-4-(thiophen-2-yl)-4H-thiopyran-3-carboxylate (9i)*

Orange oil; yield (method B): 288.9 mg (92%).  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ ): 3.78 (s, 3H,  $\text{OCH}_3$ ), 5.28 (d,  $J = 6.6$  Hz, 1H), 6.27 (d,  $J = 6.6$  Hz, 1H), 6.95 (dd,  $J = 5.4, 3.6$  Hz, 1H), 7.02 (d,  $J = 3.6$  Hz, 1H), 7.18 (d,  $J = 5.4$  Hz, 1H), 7.36–7.39 (m, 3H), 7.51–7.52 (m, 2H), 7.74 (s, 1H).  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ ): 35.9 (C(4)), 52.0 ( $\text{OCH}_3$ ), 123.6, 131.1, 137.3, 146.8 ( $4\text{C}(\text{sp}^2)$ ), 120.9, 124.6, 126.7, 126.9, 128.8, 128.9, 132.9 ( $10\text{CH}(\text{sp}^2)$ ), 164.9 (C=O). IR (film): 3060w, 2949w, 1708vs ( $\nu_{\text{C=O}}$ ), 1581m, 1432m, 1236s, 1036m, 761w, 694m. Anal. calcd for  $\text{C}_{17}\text{H}_{14}\text{O}_2\text{S}_2$  (314.43): C 64.93, H 4.50, S 20.39; found: C 64.83, H 4.73, S 20.47.

*Methyl 4-(furan-2-yl)-6-phenyl-4H-thiopyran-3-carboxylate (9j)*

Orange solid; yield (method B): 292.0 mg (98%); m.p. 75.5–76.0°C (chromatographic purification).  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ ): 3.78 (s, 3H,  $\text{OCH}_3$ ), 5.12 (d,  $J = 6.6$  Hz, 1H), 6.12 (br s, 1H), 6.20 (d,  $J = 6.6$  Hz, 1H), 6.29 (br s, 1H), 7.34–7.37 (m, 4H), 7.49 (d,  $J = 7.2$  Hz, 2H), 7.79 (s, 1H).  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ ): 35.0 (C(4)), 52.2 ( $\text{OCH}_3$ ), 121.3, 131.9, 137.4, 154.9 ( $4\text{C}(\text{sp}^2)$ ), 106.0, 110.5, 118.6, 126.6, 128.8, 129.0, 134.2, 142.0 ( $10\text{CH}(\text{sp}^2)$ ), 165.0 (C=O). IR (KBr): 3044w, 2942w, 1704vs ( $\nu_{\text{C=O}}$ ), 1591w, 1432w, 1242s, 1033w, 742m.

Anal. calcd for C<sub>17</sub>H<sub>14</sub>O<sub>3</sub>S (298.37): C 68.43, H 4.74, S 10.74; found: C 68.67, H 4.98, S 10.91.

*Methyl 4-phenyl-6-(thiophen-2-yl)-4H-thiopyran-3-carboxylate (9k)*

Orange oil; yield (method B): 222.9 mg (71%). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>): 3.70 (*s*, 3H, OCH<sub>3</sub>), 4.86 (*d*, *J* = 6.6 Hz, 1H), 6.27 (*d*, *J* = 6.6 Hz, 1H), 6.99 (*dd*, *J* = 5.4, 3.6 Hz, 1H), 7.15–7.16 (*m*, 1H), 7.22–7.24 (*m*, 2H), 7.31 (*t*, *J* = 7.2 Hz, 2H), 7.41 (*d*, *J* = 7.2 Hz, 2H), 7.72 (*s*, 1H). <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>): 41.2 (C(4)), 52.1 (OCH<sub>3</sub>), 123.2, 124.4, 140.7, 143.7 (4 C(sp<sup>2</sup>)), 121.4, 124.7, 125.3, 127.3, 127.6, 128.2, 128.9, 132.1 (10CH(sp<sup>2</sup>)), 165.1 (C=O). IR (KBr): 3025*w*, 2949*w*, 1711*vs* (ν<sub>C=O</sub>), 1587*m*, 1423*m*, 1230*s*, 1036*m*, 761*vs*. Anal. calcd for C<sub>17</sub>H<sub>14</sub>O<sub>2</sub>S<sub>2</sub> (314.43): C 64.93, H 4.50, S 20.39; found: C 64.95, H 4.77, S 20.14.

*Methyl 6-(furan-2-yl)-4-phenyl-4H-thiopyran-3-carboxylate (9l)*

Yield: 6% (method A). The compound was identified only on the basis of the <sup>1</sup>H NMR spectra and could not be isolated in pure form. The yield was calculated based on the <sup>1</sup>H NMR spectra of the crude mixture using a weighed amount of 1,1,2,2-tetrachloroethane as a standard. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>): 3.69 (*s*, 3H, OCH<sub>3</sub>), 4.84 (*d*, *J* = 6.6 Hz, 1H), 6.39–6.41 (*m*, 2H), 6.44 (*d*, *J* = 6 Hz, 1H), 7.28–7.31 (*m*, 3H), 7.36–7.39 (*m*, 3H), 7.71 (*s*, 1H). MS (ESI): *m/z* (%) = 321 (100, [M+Na]<sup>+</sup>).

*Methyl 4-phenyl-6-(selenophen-2-yl)-4H-thiopyran-3-carboxylate (9m)*

Orange oil; yield (method B): 216.4 mg (60%). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>): 3.70 (*s*, 3H, OCH<sub>3</sub>), 4.85 (*d*, *J* = 6.6 Hz, 1H), 6.22 (*d*, *J* = 6.6 Hz, 1H), 7.22–7.25 (*m*, 2H), 7.30–7.33 (*m*, 3H), 7.40–7.42 (*m*, 2H), 7.70 (*s*, 1H), 7.90 (*dd*, *J* = 6.0, 1.2 Hz, 1H). <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>): 41.4 (C(4)), 52.0 (OCH<sub>3</sub>), 124.5, 125.2, 143.6, 146.5 (4C(sp<sup>2</sup>)), 122.0, 126.9, 127.3, 128.2, 128.9, 130.1, 130.5, 132.2 (10CH(sp<sup>2</sup>)), 165.1 (C=O). IR (film): 3060*w*, 2949*w*, 1710*vs* (ν<sub>C=O</sub>), 1587*w*, 1432*m*, 1226*s*, 1040*m*, 742*m*. Anal. calcd for C<sub>17</sub>H<sub>14</sub>O<sub>2</sub>SeS (361.33): C 56.50, H 3.91, S 8.87; found: C 56.41, H 4.25, S 8.57.

*Methyl 4,6-bis(thiophen-2-yl)-4H-thiopyran (9n)*

Orange oil; yield (method A): 310.4 mg (97%). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>): 3.78 (*s*, 3H, OCH<sub>3</sub>), 5.22 (*d*, *J* = 6.6 Hz, 1H), 6.34 (*d*, *J* = 6.6 Hz, 1H), 6.92–6.93 (*m*, 1H), 6.98 (*d*, *J* = 3.6 Hz, 1H), 7.01–7.02 (*m*, 1H), 7.16 (*dd*, *J* = 5.4, 1.2 Hz, 1H), 7.20 (*dd*, *J* = 53.6, 0.6 Hz, 1H), 7.25–7.26 (*m*, 1H), 7.68 (*s*, 1H). <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>): 35.7 (C(4)), 52.2 (OCH<sub>3</sub>), 124.3, 125.0, 140.3, 146.2 (4C(sp<sup>2</sup>)), 120.0, 124.76, 124.84, 125.1, 125.7, 127.0, 127.7, 132.4 (8CH(sp<sup>2</sup>)), 164.8 (C=O). IR (film): 3041*w*, 2952*w*, 1706*vs* (ν<sub>C=O</sub>), 1581*m*, 1432*m*, 1242*s*, 1226*s*, 1024*m*, 755*w*, 701*vs*. Anal. calcd for C<sub>15</sub>H<sub>12</sub>O<sub>2</sub>S<sub>3</sub> (320.45): C 56.22, H 3.78, S 30.01; found: C 56.37, H 3.91, S 29.88.

### Disclosure statement

No potential conflict of interest was reported by the authors.

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